

US008822438B2

(12) United States Patent

Auerbach et al.

(10) Patent No.: US 8,822,438 B2 (45) Date of Patent: Sep. 2, 2014

(54) METHODS AND COMPOSITIONS FOR TREATING CANCER

(75) Inventors: Alan H. Auerbach, Hermosa Beach, CA

(US); Arie S. Belldegrum, Los Angeles,

CA (US)

(73) Assignee: Janssen Oncology, Inc., Los Angeles,

CA (US)

(*) Notice: Subject to any disclaimer, the term of this

patent is extended or adjusted under 35

U.S.C. 154(b) by 0 days.

(21) Appl. No.: 13/034,340

(22) Filed: Feb. 24, 2011

(65) **Prior Publication Data**

US 2011/0144016 A1 Jun. 16, 2011

Related U.S. Application Data

- (63) Continuation of application No. 11/844,440, filed on Aug. 24, 2007, now abandoned.
- (60) Provisional application No. 60/921,506, filed on Aug. 25, 2006.

(51) Int. Cl.

A61K 31/56 (2006.01)

A61K 31/58 (2006.01)

(56) References Cited

U.S. PATENT DOCUMENTS

2006/0030608 A1 2/2006 Nelson et al.

FOREIGN PATENT DOCUMENTS

EP 2478907 7/2012 WO 2006027266 3/2006

OTHER PUBLICATIONS

O'Donnell et al., British Journal of Cancer, 2004;90:2317-2325.* Tannock et al., J. Clin. Oncol., 1996;14:1756-1764.*

ASCO Cancer Foundation, Poster Session F: Hormone Refractory, ASCO, 2005.

Bruno et al, Targeting cytochrome P450 enzymes: A new approach in anti-cancer drug development, Elsevier, 2007, pp. 5047-5060, vol. 15

Cannell, 100th Annual Meeting of the American Association for Cancer Research, Los Angeles, CA, USA;, http://oncology.thelancet.com, 2007, pp. 471, vol. 8.

Collins, et al. "A Systematic Review of the effectiveness of Docetaxel and Mitoxantrone for the Treatement of Metastatic Hormone-Refractory Prostate Cancer", British J. of Cancer, 95, pp. 457-462 (2006). Cougar Biotechnology, Cougar Biotechnology Announces Initiation of Phase I/II Trial for CB7630 (Arbiraterone Acetate), Cougar Biotechnology, Dec. 14, 2004.

Cougar Biotechnology, Cougar Biotechnology Announces Presentation of Positive CB7630 Clinical Data at AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, Cougar Biotechnology, Oct. 2007.

Cougar Biotechnology, Cougar Biotechnology Announces Presentation of Positive CB7630 Clinical Data at ESMO Conference, Drugs. com, Jul. 2007.

Cougar Biotechnology, Cougar Biotechnology announces presentation of positive phase I and phase II data at ASCO Prostate Cancer Symposium, Cougar Biotechnology, Feb. 23, 2007.

Cougar Biotechnology, Cougar Biotechnology presents CB7630 Phase I clinical data at the 2005 Prostate Cancer Symposium, AllBusiness, 2005.

Cougar Biotechnology, Cougar Biotechnology presents positive CB7630 Clinical Data at AACR Annual Meeting Late-Breaking Clinical Trials Session, Cougar Biotechnology, Apr. 17, 2007.

Cougar Biotechnology, Cougar Technology Announces Presentation of Positive CB7630 Clinical Data at ASCO Annual Meeting, The Free Library, Jun. 4, 2007.

De Bono et al, Inhibition of CYP450c17 by abiraterone administered once daily to castrate patients with prostate cancer resistant to LHRH analogues, anti-androgens and steriod therapy is well tolerated . . . , The institute of Cancer Research, 2007.

De Coster, et al., Effects of High-Dose Ketoconazole and Dexamethason on ACTH-Stimulated Adrenal Steriodogenesis in Orchiectomized Prostatic Cancer Patients, ACTA Endocrinologica (Copenh), 1987, pp. 265-271, vol. 115.

Duc et al, In Vitro and in vivo models for the evaluation of potent inhibitors of male rat 17 -hydroxylase/C-lyase, Pergamon, 2003, pp. 537-542, vol. 84.

Endocrinology, Inhibition of Androgen Synthesis in Human Testicular and Prostatic Microsomes and in Male Rats by Novel Steroidal Compounds, Endocrinology, 1999, pp. 2891-2897, vol. 140 No. 6

Fossa, et al., Weekly Docetaxel and Prednisone Versus Prednisolone Alone in Androgen-Independent Prostate Cancer: A Randomized Phase II Study, European Urology, 2007, pp. 1691-1699, vol. 52.

Gerber, et al., Prostate Specific Antigen for Assessing Response to Ketoconazole and Prednisone in Patients with Hormone Refractory Metastatic Prostate Cancer, The Journal of Urology, 1990, pp. 1177-1179, vol. 1444, No. 5.

Hakki et al, CYP17- and CYP11B-dependent steriod hydroxylases as drug development targets, Elsevier, 2006, pp. 27-52, vol. 11.

Harris, et al., Low Dose Ketoconazole with Replacement Doses of Hydrocortisone in Patients with Progressive Androgen Independent Prostate Cancer, The Journal of Urology, 2002, pp. 542-545, vol. 168. Moreira et al, Synthesis and evaluation of novel 17-indazole androstene derivatives designed as CYP17 inhibitors, Elsevier, 2007, pp. 939-948, vol. 72.

Newell et al, The Cancer Research UK experience of pre-clinical toxicology studies to support early clinical trials with novel cancer therapies, Elsevier, 2004, pp. 899-906, vol. 40.

(Continued)

Primary Examiner — San-Ming Hui

(57) ABSTRACT

Methods and compositions for treating cancer are described herein. More particularly, the methods for treating cancer comprise administering a $17\alpha\text{-hydroxylase/C}_{17,20}\text{-lyase}$ inhibitor, such as abiraterone acetate (i.e., $3\beta\text{-acetoxy-}17\text{-}(3\text{-pyridyl})$ androsta-5,16-diene), in combination with at least one additional therapeutic agent such as an anti-cancer agent or a steroid. Furthermore, disclosed are compositions comprising a $17\alpha\text{-hydroxylase/C}_{17,20}\text{-lyase}$ inhibitor, and at least one additional therapeutic agent, such as an anti-cancer agent or a steroid.